

1 reporter being optically distinguished by said specific imaging system in response to an optical  
2 characteristic of the aggregate reporter other than size and shape.--

3 REMARKS

4 Status of the Claims

5 Claims 1-40 are now pending in the present application, new Claims 8-40 having been added and  
6 Claims 3 and 6 having been amended by the present preliminary amendment. A Supplemental Combined  
7 Declaration and Power of Attorney, executed by the inventors in this application, is submitted  
8 concurrently herewith.

9 The Examiner is requested to consider the application in the light of the above preliminary  
10 amendment. In the event that any issues arise during the course of such consideration, the Examiner  
11 is invited to telephone applicants' attorney at the number listed below.

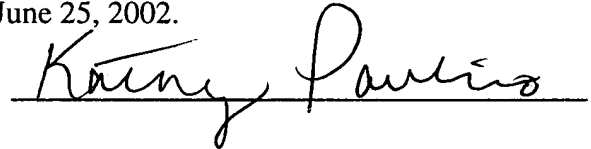
12 Respectfully submitted,

13 

14 Ronald M. Anderson  
15 Registration No. 28,829

16 I hereby certify that this correspondence is being deposited with the U.S. Postal Service in a  
17 sealed envelope as first class mail with postage thereon fully prepaid addressed to: Director of  
18 Patents and Trademarks, Arlington, VA 22202 on June 25, 2002.

19 Date: June 25, 2002

20 

21 RMA:MCK:klp

22 Enclosure

23 Supplemental Combined Declaration and Power of Attorney

1 MARKED-UP VERSION OF THE AMENDMENTS

2 Amendment to the Claims

3 In the Claims:

4 **Please amend Claims 3 and 6 as follows:**

5 3. (Amended) A method of constructing a library of uniquely identifiable reporters [labeled  
6 carriers] suitable for labeling beads to be used to generate a bead library, said method comprising the  
7 steps of:

8 (a) providing a plurality of singly labeled micro-particles, each singly labeled  
9 micro-particle comprising a uniquely identifiable characteristic;

10 (b) determining a number of unique reporters required to completely encode a  
11 desired bead library, based on the uniquely identifiable characteristics of said plurality of singly  
12 labeled micro-particles;

13 (c) providing a plurality of separate reaction vessels, including one reaction vessel  
14 for each unique reporter signature required;

15 (d) apportioning said singly labeled micro-particles among the plurality of reaction  
16 vessels, such that each reaction vessel contains at least one singly labeled micro-particle required to  
17 generate a unique reporter signature associated with that reaction vessel;

18 (e) for each reaction vessel requiring additional singly labeled micro-particles to  
19 generate a unique reporter signature associated with that reaction vessel, adding appropriate singly  
20 labeled micro-particles having a complementary chemistry until substantially all singly labeled  
21 micro-particles in that reaction vessel have combined;

22 (f) repeating step (e) in a stepwise fashion until each reaction vessel contains  
23 either a singly labeled micro-particle having a unique reporter signature associated with that reaction  
24 vessel, or a combination of singly labeled micro-particles having a unique reporter signature  
25 associated therewith.

26 6. (Amended) The method of Claim 3, further comprising the step of [using a contents of]  
27 introducing a plurality of beads into each reaction vessel to [combinatorially] generate said desired  
28 labeled bead library under conditions favorable to allowing substantially all singly labeled  
29 micro-particle or combinations of singly labeled micro-particles in the reaction vessels to attach to  
30 the plurality of beads, to produce a plurality of reporter labeled beads.

31 **Please add new Claims 8-40 as follows:**

32 --8. A method of constructing a library of optically distinct reporter labeled carriers, said  
33 method comprising the steps of:

34 (a) providing a plurality of optically distinct carriers;

35 ///

1 (b) providing a plurality of reaction vessels, such that at least one reaction vessel is  
2 available for each unique member of the library to be constructed;

3 (c) providing a plurality of optically distinct reporters;

4 (d) in each reaction vessel, apportioning at least one carrier and at least one  
5 reporter in a predetermined unique combination; and

6 (e) attaching said at least one reporter to said at least one carrier in each reaction  
7 vessel, by at least one of a physical attachment and a chemical attachment.

8 9. The method of Claim 8, wherein no reaction vessel contains a mixture of different  
9 optically distinct carriers.

10 10. The method of Claim 8, wherein said plurality of optically distinct reporters and said  
11 plurality of optically distinct carriers are optically distinguishable based on size.

12 11. The method of Claim 8, wherein said plurality of optically distinct reporters and said  
13 plurality of optically distinct carriers are optically distinguishable based on intensity.

14 12. The method of Claim 8, wherein said plurality of optically distinct reporters and said  
15 plurality of optically distinct carriers are optically distinguishable based on shape.

16 13. A method of constructing an optically discriminable reporter that is distinguishable by  
17 a specific imaging system used to optically distinguish said optically discriminable reporter,  
18 comprising the steps of:

19 (a) providing a plurality of singly labeled microparticles, each singly labeled  
20 microparticle having a uniquely identifiable optical characteristic, each singly labeled microparticle  
21 being smaller than a resolution limit of said specific imaging system employed to optically  
22 distinguish said optically discriminable reporter; and

23 (b) combining a plurality of said singly labeled microparticles together to generate  
24 an aggregate reporter having a size larger than said resolution limit, to enable the aggregate reporter  
25 to be optically distinguished by said specific imaging system.

26 14. The method of Claim 13, wherein each singly labeled microparticle comprises one of  
27 a quantum dot and a micro-bead.

28 15. The method of Claim 13, wherein the uniquely identifiable characteristic comprises a  
29 color.

30 16. The method of Claim 13, wherein the uniquely identifiable characteristic comprises an  
31 intensity.

32 17. The method of Claim 13, wherein each of the plurality of singly labeled microparticles  
33 comprising said aggregate reporter comprises has an identical uniquely identifiable characteristic.

34 18. The method of Claim 13, wherein said aggregate reporter comprises at least two groups of  
35 singly labeled microparticles each group having a different uniquely identifiable characteristic.

1           19.    A method of constructing a plurality of reporters comprising the steps of:  
2               (a)    providing a plurality of singly labeled microparticles that individually are  
3 incapable of functioning as reporters, each singly labeled microparticle having a uniquely identifiable  
4 characteristic, each singly labeled microparticle being smaller than a resolution limit of an imaging  
5 system that is to be employed to optically distinguish said plurality of reporters;  
6               (b)    determining a number of unique reporters desired, each unique reporter being  
7 indicated by the uniquely identifiable characteristics of said plurality of singly labeled microparticles;  
8               (c)    providing a plurality of separate reaction vessels, such that a different separate  
9 reaction vessel is provided for each unique reporter desired, each separate reaction vessel being  
10 associated with a different unique reporter;  
11              (d)    apportioning said singly labeled microparticles among the plurality of reaction  
12 vessels, such that each reaction vessel contains at least one of each singly labeled microparticle  
13 required to generate a unique reporter signature associated with that reaction vessel;  
14              (e)    for each reaction vessel other singly labeled microparticles to generate the  
15 unique reporter signature associated with that reaction vessel, adding the other singly labeled  
16 microparticles until substantially all singly labeled microparticles in that reaction vessel have  
17 combined; and  
18              (f)    repeating step (e) in a stepwise fashion until each reaction vessel contains an  
19 aggregate of singly labeled microparticle defining the unique reporter signature associated with that  
20 reaction vessel.  
21           20.    The method of Claim 19, wherein each singly labeled microparticle comprises one of  
22 a quantum dot and a micro-bead.  
23           21.    The method of Claim 19, wherein the uniquely identifiable characteristic is a color.  
24           22.    The method of Claim 19, wherein the uniquely identifiable characteristic is an  
25 intensity.  
26           23.    The method of Claim 19, wherein the uniquely identifiable characteristic is a shape.  
27           24.    A method of preparing a library of diverse compounds, each compound including a  
28 plurality of components and being produced by a combination of a directed synthesis and a  
29 combinatorial synthesis, said method comprising the steps of:  
30               (a)    providing a plurality of optically distinct carriers;  
31               (b)    providing a plurality of reaction vessels, such that a different reaction vessel is  
32 available for each different type of optically distinct carrier;  
33               (c)    apportioning said plurality of optically distinct carriers among said plurality  
34 of reaction vessels, such that each reaction vessel contains only one type of optically distinct  
35 carrier;

1 (d) in each of said plurality of reaction vessels, performing a directed synthesis by  
2 exposing said optically distinct carriers to a plurality of first components until substantially all  
3 optically distinct carriers have coupled to at least one first component, a different first component  
4 being added to each reaction vessel, such that each type of optically distinct carrier identifies a  
5 different first component;

6 (e) pooling contents from each reaction vessel, to form a common pool comprising  
7 said plurality of optically distinct carriers;

8 (f) apportioning the common pool among said plurality of reaction vessels, such  
9 that each reaction vessel contains a mixture of different optically distinct carriers and first  
10 components;

11 (g) in each reaction vessel, exposing each mixture to a plurality of optically  
12 distinct first reporters, until substantially all optically distinct carriers have at least one optically  
13 distinct first reporter coupled thereto, a different optically distinct first reporter being added to each  
14 reaction vessel; and

15 (h) performing a combinatorial synthesis by exposing each mixture of different  
16 optically distinct carriers, different first components, and different optically distinct first reporters in  
17 each reaction vessel to a plurality of second components, until substantially all optically distinct  
18 carriers have at least one second component coupled thereto, a different second component being  
19 added to each reaction vessel, such that each different optically distinct first reporter identifies a  
20 different second component.

21 25. The method of Claim 24, wherein after the step of exposing each mixture of different  
22 optically distinct carriers, different first components and different optically distinct first reporters to a  
23 plurality of second first components, further comprising the steps of:

24 (a) pooling the contents of each reaction vessel to form a second common pool;

25 (b) apportioning said second pool among said plurality of reaction vessels, such  
26 that each reaction vessel contains a second mixture of different optically distinct carriers, first  
27 components, optically distinct first reporters, and second components;

28 (c) in each reaction vessel of said plurality of reaction vessels, exposing each  
29 second mixture of different optically distinct carriers, first components, first reporters, and second  
30 components to a plurality of optically distinct second reporters, until substantially all optically  
31 distinct carriers have at least one optically distinct second reporter coupled thereto, a different second  
32 optically distinct reporter being added to each reaction vessel; and

33 (d) performing a combinatorial synthesis by exposing each second mixture of  
34 different optically distinct carriers, first components, optically distinct first reporters, second  
35 components, and optically distinct second reporters to a plurality of third components, until

1 substantially all optically distinct carriers have at least one third component coupled thereto, a  
2 different third component being added to each different reaction vessel, such that each type of  
3 optically distinct second reporter identifies a different third component.

4 26. The method of Claim 25, further comprising the step of repeating the steps of pooling,  
5 apportioning, exposing to a different reporter, and exposing to a different component, as in Claim 25,  
6 until a desired number of components have been added to said plurality of optically distinct carriers.

7 27. The method of Claim 24, wherein said plurality of optically distinct carriers are  
8 optically distinguishable based on size.

9 28. The method of Claim 24, wherein said plurality of optically distinct carriers are  
10 optically distinguishable based on intensity.

11 29. The method of Claim 24, wherein said plurality of optically distinct carriers are  
12 optically distinguishable based on shape.

13 30. The method of Claim 24, wherein each different optically distinct reporter is optically  
14 distinguishable based on size.

15 31. The method of Claim 24, wherein each different optically distinct reporter is optically  
16 distinguishable based on light intensity.

17 32. The method of Claim 24, wherein each different optically distinct reporter is optically  
18 distinguishable based on shape.

19 33. The method of Claim 24, wherein after the step of exposing each mixture of different  
20 optically distinct carriers, different first components and different optically distinct first reporters to a  
21 plurality of second components, further comprising the steps of:

22 (a) pooling the contents of each reaction vessel to form a second common pool;

23 (b) apportioning said common pool among less than all of said plurality of  
24 reaction vessels, such that at least one reaction vessel remains empty, and that a remainder of the  
25 plurality of reaction vessels each contains the mixture of different optically distinct carriers, first  
26 components, first optically distinct reporters, and second components;

27 (c) in each of the remainder of reaction vessels, exposing each mixture of different  
28 optically distinct carriers, first components, first optically distinct reporters, and second components  
29 to a plurality of optically distinct second reporters, until substantially all optically distinct carriers are  
30 coupled to at least one optically distinct second reporter, a different second reporter being added to  
31 each of the remainder of the reaction vessel; and

32 (d) performing a constrained combinatorial synthesis in each of the remainder of the  
33 reaction vessels by exposing each mixture of different optically distinct carriers, first components, first  
34 optically distinct reporters, second components and second optically distinct reporters to a plurality of  
35 third components, until substantially all optically distinct carriers are coupled to at least one third

1 component, a different third component being added to each of the remainder of the reaction vessels, such  
2 that each type of optically distinct second reporter identifies a different third component.

3 34. A method of preparing a library of diverse compounds by a step-wise synthesis, each  
4 compound including a plurality of components, comprising the steps of:

5 (a) providing a plurality of reaction vessels, such that a different reaction vessel is  
6 provided for each different compound to be prepared;

7 (b) providing a plurality of optically distinct carriers of different types, fewer  
8 different types of optically distinct carriers being provided than a number of the reaction vessels that  
9 are provided;

10 (c) apportioning said plurality of optically distinct carriers among said plurality of  
11 reaction vessels, such that at least two reaction vessels contain an identical type of optically distinct  
12 carrier;

13 (d) in each reaction vessel of said plurality of reaction vessels, exposing said  
14 optically distinct carriers to a plurality of first components, until substantially all optically distinct  
15 carriers have at least one first component coupled thereto, identical first components being added to  
16 each reaction vessel that contains the identical type of optically distinct carrier; and

17 (e) in each reaction vessel of said plurality of reaction vessels, exposing said  
18 optically distinct carriers to a plurality of second components, until substantially all optically distinct  
19 carriers coupled to at least one second component, identical second components being added to each  
20 reaction vessel that contains the identical type of optically distinct carrier, such that each different  
21 type of optically distinct carrier uniquely identifies a specific combination of first and second  
22 components.

23 35. The method of Claim 34, wherein after the step of exposing said optically distinct  
24 carriers to a plurality of second components, further comprising the steps of:

25 (a) in each reaction vessel, exposing said optically distinct carriers to a plurality of  
26 third components, until substantially all optically distinct carriers are coupled to at least one third  
27 component, different types of third components being added to each reaction vessel that contains the  
28 identical type of optically distinct carrier; and

29 (b) in each reaction vessel, exposing said optically distinct carriers to a plurality of  
30 optically distinct first reporters, until substantially all optically distinct carriers are coupled to at least  
31 one first optically distinct first reporter, an identical optically distinct first reporter being added to  
32 each reaction vessel containing the same third component, such that each type of optically distinct  
33 first reporter identifies a different third component.

34 36. The method of Claim 35, wherein in each reaction vessel, after the step of exposing  
35 said optically distinct carriers to a plurality of optically distinct first reporters, further comprising the

1 step of exposing said optically distinct carriers to a plurality of fourth components, until substantially  
2 all optically distinct carriers are coupled to have at least one fourth component, the identical type of  
3 fourth component being added to each reaction vessel, such that each type of optically distinct first  
4 reporter uniquely identifies a specific combination of third and fourth components.

5 37. A method of preparing a library of different compounds by a step-wise synthesis, each  
6 compound including at least one component and being uniquely identified by a plurality of optically  
7 distinct reporters, said plurality of optically distinct reporters being added in a single portion of said  
8 step-wise synthesis, said method comprising the steps of:

9 (a) providing a plurality of carriers;  
10 (b) providing a plurality of reaction vessels, such that a separate reaction vessel is  
11 provided for each different compound to be prepared;

12 (c) providing a plurality of optically distinct reporters of different types, such that  
13 a sufficient number of different types of optically distinct reporters are provided so as to enable each  
14 different compound to be prepared to be uniquely identifiable using a unique combination of  
15 optically distinct reporters;

16 (d) apportioning said plurality of carriers among said plurality of reaction vessels;

17 (e) in each reaction vessel, exposing said plurality of carriers contained therein to a  
18 different combination of optically distinct reporters, until substantially all carriers are coupled to at least  
19 one combination of optically distinct reporters, carriers in different reaction vessels thus exposed having  
20 different optical signatures, due to the different combination of optically distinct reporters; and

21 (f) in each reaction vessel, exposing said plurality of carriers to a plurality of first  
22 components, until substantially all of the plurality of carriers are coupled to at least one first  
23 component.

24 38. The method of Claim 37, wherein for each reaction vessel that was provided for a  
25 compound that requires at least another component, further comprising the step of exposing said  
26 plurality of carriers to any other components thus required, in a step-wise fashion, until each reaction  
27 vessel contains the compound for which the reaction vessel was provided.

28 39. A method of preparing a library of different compounds by a step-wise synthesis, each  
29 different compound being uniquely identified by a plurality of optically distinct reporters, said  
30 method comprising the steps of:

31 (a) providing a plurality of carriers;

32 (b) providing a plurality of reaction vessels, such that a separate reaction vessel is  
33 provided for each different compound to be prepared;

34 (c) providing a plurality of optically distinct reporters of different types, such that  
35 a sufficient number of different types of optically distinct reporters are provided so as to enable each



1 different compound to be prepared to be uniquely identifiable using a unique combination of  
2 optically distinct reporters;

3 (d) apportioning said plurality of carriers among said plurality of reaction vessels;

4 (e) in each reaction vessel of said plurality of reaction vessels, exposing said  
5 plurality of carriers to a different combination of optically distinct reporters, until substantially all of  
6 the plurality of carriers are coupled to at least one combination of optically distinct reporters, carriers  
7 from different reaction vessels comprising different optical signatures, due to the different  
8 combination of optically distinct reporters added to each reaction vessel; and

9 (f) in each reaction vessel, exposing said plurality of carriers to a plurality of  
10 compounds, until substantially all of the plurality of carriers are coupled to at least one compound  
11 coupled, a different compound being added to each reaction vessel.

12 40. A method of constructing an optically discriminable reporter that is distinguishable by  
13 a specific imaging system used to optically distinguish said optically discriminable reporter,  
14 comprising the steps of:

15 (a) providing a plurality of singly labeled microparticles, each singly labeled  
16 microparticle having a uniquely identifiable optical characteristic, each singly labeled microparticle  
17 being smaller than a resolution limit of said specific imaging system employed to optically  
18 distinguish said optically discriminable reporter; and

19 (b) combining a plurality of said singly labeled microparticles together to generate  
20 an aggregate reporter having a size that is still smaller than said resolution limit, the aggregate  
21 reporter being optically distinguished by said specific imaging system in response to an optical  
22 characteristic of the aggregate reporter other than size and shape.--  
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